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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,695	03/29/2002	Dirk Gerrit Meuleman	0/97263 US	5130

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/380,695	MEULEMAN ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Receipt of applicants' amendments and remarks submitted September 15, 2004 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haenggi et al. (of record).

3. Haenggi et al. treated postmenopausal women with Tibolone with a daily amount of 2.5 mg (page 646, Patients and Methods), which meet the effective amount herein (see page 6, lines 25-30 herein in the specification). Haenggi et al. teach that tibolone is known to be used as hormone replace therapy in postmenopausal women. See, pages 648-649.

4. Haenggi et al. do not teach expressly teach that the postmenopausal women are suffering from atherosclerosis.

5. However, it have been well understood in the art that substantial portion of the population of postmenopausal women are suffering atherosclerosis.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treat postmenopausal women because there is no obvious reasons for not using the hormone replace therapy in postmenopausal women suffering from atherosclerosis.

6. As to the functional limitation recited in the preamble herein, "inhibiting the atherosclerotic process," note the instant claims are directed to affecting a biochemical pathway with an old and well-known compound. The argument that such claims are not directed to the old and well known ultimate utility (administering postmenopausal women) for the compounds, e.g., Tibolone, are not probative. It is well settled patent law that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter. Applicant's attention is directed to In re Swinehart, (169 USPQ 226 at 229) where the Court of Customs and Patent Appeals stated "is elementary that the mere recitation of a newly discovered function or property, inherently possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." In the instant invention, the claims are directed to the ultimate utility set forth in the prior art, albeit distanced by various biochemical functions. The ultimate utility for the claimed compounds is old and well known rendering the claimed subject matter obvious to the skilled artisan. It would follow therefore that the instant claims are properly rejected under 35 USC 103.

7. Claims 1-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haenggi et al. (of record), in view of Berglund.

8. Haenggi et al. teaches a method of decreasing lipoprotein (a) by administering 7alpha-methyl-17alpha-ethynyl-17beta-hydroxy-5(10)-estren-3-one (Tibolone), to a human subject, see the entire document, the abstract in particular. Haenggi further teaches that Lp(a) has been shown to be a strong independent risk factor for coronary disease, see the abstract. Haenggi also teach a method of treating postmenopausal women with Tibolone in an effective amounts herein defined. (page 646, Patients and Methods, and page 6, lines 25-30 herein in the specification).

9. Haenggi et al. does not teach expressly the employment of Tibolone in a method of inhibiting atherosclerosis.

10. However, Berglund teaches that Lp(a) has been implicated with an increased risk of atherosclerosis, see the abstract.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ Tibolone in a method of inhibiting atherosclerosis, e.g., by administering to a subject being suffering from atherosclerosis Tibolone.

A person of ordinary skill in the art would have been motivated employ Tibolone in a method of inhibiting progress of atherosclerosis because Lp(a) has been implicated an increased risk of atherosclerosis, and lowering the level of lipoprotein (a) would have reasonably expected to inhibit the progress of atherosclerosis.

2. Further, it would have been obvious to one of ordinary skill in the art, at the time the claimed invention was made, to use the method of Haenggi et al. to postmenopausal women suffering from atherosclerosis since Haenggi et al. should tibolone would provide some benefit for inhibiting the progress of atherosclerosis, as discussed above.

Response to the Arguments

Applicants' amendments and remarks submitted September 15, 2004 have been fully considered, but are not persuasive as to the rejections set forth above.

Applicants argue that the instant claims are not obvious over Haenggi et al. because it is known that Tibolone also decrease the HDL-cholesterol. The arguments are improper. Particularly, the cited prior arts established that Lp(a) is closely associated with atherosclerosis, therefore, decrease of Lp(a) would have been reasonably expected to suppress, or inhibit the

development of atherosclerosis. Applicants argue that Tibolone decrease HDL-cholesterol, however, fails to establish the relationship of the decrease of HDL-cholesterol and atherosclerosis. Applicants fails to establish a prima facie case that decrease of HDL-cholesterol would have discourage one of ordinary skill in the art from using Tibolone for inhibiting atherosclerosis. Note, Haenggi et al. merely teaches that lowering lipoprotein (a) would counter balance the adverse effect of tibolone on other lipoprotein risk factors. There is no teaching as to the relation of those factors and atherosclerosis. Further, even if it is known that decrease of HDL-cholesterol is associated with atherosclerosis, there is no sufficient evidence to show that the decrease of HDL-cholesterol would out weight the benefit of lowing Lp(a), particularly, in view the fact that Lp(a) has been shown to be a strong independent risk factor for coronary heart disease.

11. Applicants contend that the instant claims are based on the discovery of unexpected benefit resided in the claims. The arguments are not persuasive. The examiner fails to see the alleged "unexpected" results. Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). The claims must be commensurate in the scope with any evidence of unexpected results. See MPEP 716.02 (d). The claims are directed to mammal in general, and in human in particular. The data is based on rabbit, which, applicants admitted, is different from other mammal, such as human (Lp(a) not present, page 6 of the response submitted December 30, 2003). There is no reasonable expectation that such unexpected result would be extrapolated to other mammal. Therefore, the unexpected results are not commensurate with the scope herein claimed. Further,

it is contend that, in view the fact that substantial portion of postmenopausal women have atherosclerosis, treating menopausal women suffering from atherosclerosis would have been obvious over Heanggi et al.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617